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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/925,627	09/09/97	FAUSTMAN D	00786/036005

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EXAMINER	
SCHEINER, L	
ART UNIT	PAPER NUMBER
1648	18

DATE MAILED: 04/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
08/925,627	Faustman
Examiner	**Art Unit**
Lauri Schein r	1648

-- Th MAILING DATE of this communicati n app ars on th c v r sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Feb 15, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 36, 39-43, 47, 57, 59, 60, and 89-97 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 36, 39-41-43, 47, 57, 59, 60, and 89-97 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Claims 36, 39-43, 47, 57, 59, 60 and 89-97 are pending in this application.

Applicant's arguments with respect to claims 36, 39-43, 47, 57, 59 and 60 have been considered but are moot in view of the new ground(s) of rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 89-91 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and as failing to provide an adequate written description of the invention and failing to present the best mode contemplated by the applicant for carrying out his invention.

The specification fails to enable the recitation of "wherein said composition comprises a genetically engineered cell" in newly added claims 89-91. That is, with respect to making and using, the specification fails to provide any meaningful guidance to one of skill. The specification is directed to teaching the prevention of tissue rejection by antibody masking of islet MHC class I antigens prior to transplantation. However, the term "genetically engineered" is merely mentioned in the context of transplantation of genetically engineered liver cells which secrete factor VIII into hemophilia recipients. Again, guidance is lacking. Moreover, the written description requirement under Section 112, first paragraph, sets forth that the claimed subject matter must be supported by an adequate written description that is sufficient to enable anyone skilled in the art to make and use the invention. *In re Rasmussen,* 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim,* 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). The courts have concluded that the specification must demonstrate that the inventor(s) had

possession of the claimed invention as of the filing date relied upon. Although the claimed subject matter need not be described identically, the disclosure relied upon must convey to those skilled in the art that applicants had invented the subject matter claimed. *In re Wilder, et al.,* 222 U.S.P.Q. 369 (C.A.F.C. 1984). *In re Werthheim, et al.,* 191 U.S.P.Q. 90 (C.C.P.A. 1976). *In re Driscoll,* 195 U.S.P.Q. 434 (C.C.P.A. 1977). *Utter v. Hiraga,* 6 U.S.P.Q.2d 1709 (C.A.F.C. 1988). *University of California v. Eli Lilly,* 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). *Fiers v. Sugano,* 25 U.S.P.Q.2d 1601-1607 (C.A.F.C. 1993). The specification is devoid of any substantive guidance which would enable one of ordinary skill in the art to make and use the invention commensurate with that which is claimed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36, 39-43, 47, 57, 59, 60 and 92-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stock et al.(Journal of Surgical Research **46**, 317-321 (1989) in view of Faustman et al. (PNAS USA 78(1981)).

Stock et al. teach that the pretreatment of B10.BR (H-2^k) and DBA/2J (H-2^d) islets with an allospecific anti-MHC class I monoclonal antibody blocked the generation of allospecific CTL when the pretreated islets were placed into coculture with C57B1/6 (H-2^b) splenocytes.

Stock et al. differ from the instant invention in failing to teach compositons comprising human islets or human islets as replacements for murine islets in their *in vitro* preliminary transplantation assays.

Faustman et al. (although having an earlier publication date than Stock et al.) is somewhat cumulative. However, Faustman et al. differ from Stock et al. in teaching pretreatment of murine islets with antisera, as well as additionally teaching *in vivo* islet allotransplantation. Faustman et al. are cited for addressing limitations to the claims wherein the antigen is masked with at least two masking agents obtained from polyclonal antisera raised against the antigen, as well as for providing cumulative state of the art evidence. Thus, Faustman et al. is not cited for curing the deficiency of Stock et al.

Again, applicant's claims are drawn to a transplantable composition for use in humans. It is noted that although applicant's specification does teach a capped HLA class I positive human islet composition, the transplantation is xenogeneic. Thus, it is asserted that the functionally equivalent substitution of human islets for murine islets (and the appropriate corresponding antibody) of Stock et al. or Faustman et al. (allogeneic -> xenogeneic) would have been obvious as a next step in further understanding human islet antirejection, just as the next obvious step after the substitution of human islets for murine islets would be a human allogeneic transplantation assay. Thus, the allogeneic assays set forth by the respective references in many respects more closely parallel the future human allogeneic assays referenced by Stock et al. and Faustman et al. than the xenogeneic assay of the instant disclosure. It is additionally noted that where it is recognized that two components are equivalent, an express suggestion to substitute one for another need not be present in the applied reference in order to render such substitution obvious. In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982). It is asserted that murine islets and human islets are recognized to be equivalent since the murine model is routinely used for the study of diabetes in humans.

Thus it would have been obvious for one of ordinary skill in the art at the time of the invention to mask human donor islets with mouse antibodies to human islets prior to transplantation since the results of Faustman et al. indicate that pretreatment of allogeneic mouse islets with donor-specific Ia antiserum and complement results in the prevention of their immune rejection in nonimmunosuppressed mice for at least 200 days after transplantation. Additionally, Faustman et al. teach that the elimination of the need for immunosuppression of the host is an important advance, particularly with regard to the eventual application of islet transplantation to the treatment of diabetes in **man**. Similarly, Stock et al. teach that if such a pretreatment regiment is similarly effective *in vivo*, it could be potentially used as an antirejection strategy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Scheiner, whose telephone number is (703) 308-1122. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

Laurie Scheiner/LAS
April 21, 2001

LAURIE SCHEINER
PRIMARY EXAMINER